

AMENDMENT

In the Claims

~~Please cancel claims 59-109 and insert therefore:~~

~~110.~~ A composition, comprising:

a nucleic acid comprising a polynucleotide selected from the group consisting of a polynucleotide which is anti-sense to a target polynucleotide and/or a sense polynucleotide encoding a protein;

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an adjuvant selected from the group consisting of hyaluronic acid and derivatives thereof;
and

a pharmaceutically acceptable carrier.

111. The composition of claim 110, wherein the nucleic acid comprises a polynucleotide which is anti-sense to a target polynucleotide.

112. The composition of claim 111, wherein the target polynucleotide is selected from the group consisting of genomic DNA, cDNA, messenger RNA (mRNA) and an oligonucleotide.

113. The composition of claim 110, wherein the nucleic acid is operatively linked to a vector.

114. The composition of claim 113, wherein the polynucleotide linked to the vector comprises a sense polynucleotide encoding a protein.

115. The composition of claim 113, wherein the polynucleotide linked to the vector comprises an anti-sense polynucleotide.

116. The composition of claim 113, wherein the vector is a virus.

D (cont'd)
117. The composition of claim 116, wherein the virus is selected from the group consisting of adenoviruses, adeno-associated viruses, herpes viruses and retroviruses.

117. The composition of claim 116, wherein the virus is a replication-defective adenovirus.

118. The composition of claim 117, where the replication-defective adenovirus comprises a promoter selected from the group consisting of a respiratory syncytial virus promoter, a cytomegalovirus promoter, an adenovirus major late protein (MLP), and VA1 pol III and β -actin promoters.

119. The composition of claim 118, wherein the replication-defective adenovirus comprises a promoter selected from the group consisting of a respiratory syncytial virus promoter and a cytomegalovirus promoter.

120. The composition of claim 113, wherein the vector is selected from the group consisting of pAd.RSV, pAd.MLP and pAdVA1.

121. The composition of claim 113, wherein the vector is selected from the group consisting of Ad.RSV.αVEGF and AdVA1αVEGF.

122. The composition of claim 113, wherein the vector further comprises a polyadenylation signal sequence.

D
contd 123. The composition of claim 122, wherein the polyadenylation signal sequence comprises an SV40 signal sequence.

~~124.~~ A composition comprising a nucleic acid comprising:

a polynucleotide of 7 to 50 nucleotides long, which is anti-sense to at least a portion of a polynucleotide encoding a vascular endothelial growth factor (VEGF);

and a pharmaceutically-acceptable carrier.

125. The composition of claim 124, further comprising an adjuvant selected from the group consisting of adjuvants which increase cellular uptake.

126. The composition of claim 125, wherein the adjuvant is selected from the group consisting

of hyaluronic acid and derivatives thereof.

127. The composition of claim 124, wherein the anti-sense polynucleotide has 148% complementarity to a portion of the gene encoding VEGF.
128. The composition of claim 124, wherein the anti-sense polynucleotide is 16 to 50 nucleotides long.
129. The composition of claim 128, wherein the anti-sense polynucleotide is from 7 to 22 nucleotides long.

D²(cont'd)

130. The composition of claim 128, wherein the anti-sense polynucleotide is from 7 to 19 nucleotides long.
131. The composition of claim 124, wherein:
the nucleic acid is operatively linked to a viral vector; and
the anti-sense polynucleotide is from about 20 nucleotides long to the full length of the sense polynucleotide encoding VEGF.
132. The composition of claim 124, further comprising an adjuvant.

133. The composition of claim 124, wherein the adjuvant is selected from the group consisting of hyaluronic acid and derivatives thereof.

134. The composition of claim 124, wherein the anti-sense polynucleotide is from about 50 nucleotides long to the full length sense polynucleotide encoding VEGF.

135. The composition of claim 131, wherein the sense polynucleotide encodes a VEGF selected from the group consisting of human retinal pigment epithelial cell VEGF and human choroidal endothelial cell VEGF.

D²(contd)

~~136.~~ A composition comprising:

a virus operatively linked to a nucleic acid comprising a polynucleotide which is complementary to a sense polynucleotide encoding at least a portion of a vascular endothelial growth factor (VEGF), the virus being capable of integrating the anti-sense polynucleotide into the genome of a target cell; and

a pharmaceutically-acceptable carrier.

137. The composition of claim 136, further comprising an adjuvant.

138. The composition of claim 137, wherein the adjuvant is selected from the group consisting of hyaluronic acid and derivatives thereof.

139. The composition of claim 136, wherein the virus is an adeno-associated virus.

140. The composition of claim 136, wherein the anti-sense polynucleotide is from about 20 nucleotides long to the full length VEGF-encoding sense polynucleotide.

141. The composition of claim 140, wherein the anti-sense polynucleotide is at least about 50 nucleotides long.

D¹(contd)

142. A method of treating a retinal disease associated with abnormal neovascularization, comprising administering a composition comprising an amount of a nucleic acid comprising a polynucleotide which is anti-sense to at least a portion of a sense polynucleotide encoding a vascular endothelial growth factor (VEGF), and one or more adjuvants for increasing cellular uptake, wherein said adjuvants includes at least hyaluronic acid or derivatives thereof into the eye(s) of a subject in need of such treatment, effective to inhibit or reduce neovascularization.

143. The method of claim 142, wherein the anti-sense polynucleotide is 7 to 50 nucleotides long.

144. The method of claim 143, wherein the anti-sense polynucleotide is at least 16 nucleotides long.

145. The method of claim 144, wherein the anti-sense polynucleotide is up to 22 nucleotides long.

~~146.~~ A method of treating a retinal disease associated with abnormal neovascularization, comprising the acute administration to a subject in need of such treatment of a composition comprising:

D² (cont'd)
a nucleic acid comprising a polynucleotide selected from the group consisting of a polynucleotide which is anti-sense to a target polynucleotide and/or a sense polynucleotide encoding a protein, wherein said polynucleotide is operatively linked to a vector;

an adjuvant selected from the group consisting of hyaluronic acid and derivatives thereof; and

a pharmaceutically acceptable carrier,

in an amount of the nucleic acid effective to inhibit or reduce abnormal neovascularization.

~~147.~~ A long-term method of treating a retinal disease associated with abnormal neovascularization, comprising chronically administering to the eye(s) of a subject in need of such treatment a composition comprising:

a virus operatively linked to a nucleic acid comprising a polynucleotide which is complementary to a sense polynucleotide encoding at least a portion of a vascular endothelial growth factor (VEGF), the virus being capable of integrating the anti-sense polynucleotide into the genome of a target cell; and

a pharmaceutically-acceptable carrier,

D¹(contd)
in an amount of the nucleic acid effective to inhibit or reduce neovascularization.

~~148.~~ A long-term method of treating a retinal disease associated with abnormal neovascularization, comprising chronically administering into the eye(s) of a subject in need of such treatment a composition comprising

a virus operatively linked to a nucleic acid comprising a polynucleotide which is complementary to a sense polynucleotide encoding at least a portion of a vascular endothelial growth factor (VEGF), the virus being capable of integrating the anti-sense polynucleotide into the genome of a target cell; and

a pharmaceutically-acceptable carrier,

in an amount of the nucleic acid effective to inhibit or reduce neovascularization.

149. The method of claim 142, wherein the retinal disease is selected from the group consisting of age-related macular degeneration, diabetic retinopathy, branch or central retinal vein occlusion, retinopathy of prematurity, rubeosis iridis and corneal neovascularization.

~~150.~~ A method of promoting uptake of an exogenous nucleic acid by a target cell, comprising contacting a target cell with a nucleic acid or with a virus or vector operatively linked to the nucleic acid, in the presence of an adjuvant selected from the group consisting of hyaluronic acid and derivatives thereof.

D² cont'd)

151. The method of claim 150, wherein the target cell is a phagocytic cell.

152. The method of claim 150, wherein the nucleic acid, the virus or the vector, and the adjuvant are contacted with the cell *in vitro*.

153. The method of claim 152, wherein the nucleic acid and the adjuvant are contacted with the cell in the form of a composition.

154. The method of claim 152, wherein the nucleic acid, the virus or the vector, and the adjuvant are administered to a subject *in vivo*.

155. The method of claim 154, wherein the nucleic acid, the virus or the vector, and the adjuvant are administered to the subject in the form of a composition.